REMARKS

Claims 12-19 and 38 are currently pending. Claims 12, 13, 15-17, 19 and 38 have been amended. After entry of the instant amendment, claims 12-19 and 38 will be pending.

Claim 12 has been amended to clarify the conditions under which the recited nucleotide sequences of part (b) and part (c) hybridize to a second recited nucleic acid molecule. Support for this amendment can be found on page 27, lines 10-13, of the specification. Claim 12 has also been amended to clarify that the nucleotide sequences encompassed by parts (b) and (c) must additionally encode an amino acid sequence that is at least 80% identical to SEQ ID NO: 2. This corrects an editorial oversight. No new matter has been added.

Claims 12, 13, 15-17, 19 and 38 have been amended to correct additional editorial oversights. No new matter has been added.

Objection to the Title

The title was objected to for allegedly not being descriptive of the elected invention. The title of the application is herein amended to read as follows: POLYNUCLEOTIDES ENCODING COCCIDIAN PARASITE CASEIN KINASE I, A CHEMOTHERAPEUTIC TARGET FOR ANTIPROTOZOAL AGENTS.

Objections to the Specification

The Office Action requests that Applicants confirm that "the specification, file-date of June 6, 2008, and annotated WO/2005/070180 and PCT/US2005/000955, is the currently pending specification." Applicants confirm that the PCT application publication no. and serial no., WO2005/070180 and PCT/US2005/000955, respectively, noted in the Office Action correspond to the instant national phase application. However, please note that the PCT application was filed on January 12, 2005, not on June 6, 2008, and claims priority to US provisional application serial no. 60/537,094, filed January 16, 2004.

The Office Action further requests that the specification be updated to reflect the current status of all parent applications. Please note that the section of the specification entitled "CROSS-REFERENCE TO RELATED APPLICATIONS" on page 1 was updated by a preliminary amendment submitted upon filing the instant national phase application, and should read as follows:

> The present application is the national stage entry of PCT International Application No. PCT/US2005/000955, having an international filing date of January 12, 2005, which claims the benefit of priority to U.S. Provisional Application No. 60/537,094, filed January 16, 2004, hereby incorporated by reference herein.

This updated information is still current.

The specification was objected to for containing internal hyperlinks. The specification has been reviewed and amended to delete the one hyperlink identified.

Rejection of Claims 12-19 and 38 under 35 U.S.C. § 112, 2nd Paragraph

Claim 12 was rejected under 35 U.S.C. § 112, 2nd paragraph, for containing the phrase "moderate to high stringency." Applicants have amended the stringency language of parts (b) and (c) of claim 12, specifying the hybridization conditions for moderate (for part (c)) and high (for part (b)) stringency. Support can be found on page 27, lines 10-13, of the specification.

Claims 12, 16, 17 and 38 were rejected for containing the phrase "an amino acid sequence as set forth in SEQ ID NO: 2," "an amino acid sequence of SEQ ID NO: 2," and/or "a nucleic acid sequence of SEQ ID NO: 1" (emphasis added). Claims 12, 16, 17 and 38 have been amended to change the "an" or "a" to "the." Claims 13 and 17 were similarly rejected for containing the phrase "a nucleic acid molecule of claim . . . " (emphasis added) and have been amended to change the "a" to "the."

Claims 15 and 19 were rejected for containing the phrase "the host cells of step (a)" (emphasis added). As suggested by the Examiner, this phrase has been amended to read as "the host cell of step (a)."

Rejection of Claim 12 under 35 U.S.C. § 112, 1st Paragraph

I. Enablement

Claim 12 was rejected under 35 U.S.C. § 112, 1st paragraph for allegedly lacking enablement. While acknowledging enablement for a polynucleotide encoding SEQ ID NO: 2, the Office Action states that the specification does not reasonably provide enablement for any polynucleotide encoding any CKI protein having at least 80% identity to SEQ ID NO: 2" (p. 5). The Office Action further states that "Claim 12 is so broad as to encompass any polynucleotide having at least 80% activity with SEQ ID NO: 2 and having any CKI 'multipotential serine/threonine protein kinase activity" (p. 5). Applicants respectfully traverse.

Applicants initially point out that claim 12, as currently amended, is drawn to a genus of purified nucleic acid molecules which includes nucleotide sequences that encode the protein of SEQ ID NO: 2 (part (a)) and nucleotide sequences that hybridize either under high stringency conditions to the complement of a nucleic acid molecule encoding SEQ ID NO:2 (part (b)) or under moderate stringency conditions to the complement of SEQ ID NO: 1 (part (c)). The 80% identity limitation further defines the nucleotide sequences included within parts (b) and (c) of the genus claim. Thus, only those nucleotide sequences that either (1) encode SEQ ID NO: 2 or (2) hybridize under the conditions recited in parts (b) and (c) and encode an amino acid sequence 80% identical to SEQ ID NO: 2 are included within the genus. This is contrary to the Office Action's finding that claim 12 encompasses "any CKI protein having at least 80% identity to SEQ ID NO: 2."

The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. U.S. v. Telectronics Inc., 857 F.2d 778 (Fed. Cir. 1988). One skilled in the art is presumed to use the information available to him in attempting to make or use the claimed invention, precluding the need to set forth well-known subject matter or every detail related to the invention in the application. See Northern Telecom, Inc. v. Datapoint Corp. 908 F.2d 931 (Fed. Cir. 1990); DeGeorge v. Bernier, 768 F.2d 1318 (Fed. Cir. 1985).

Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field, and the factors that can be considered in determining whether an amount of experimentation is undue have been listed in In re Wands, 858 F.2d 731 (Fed. Cir. 1988). Importantly, the test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, so long as it is merely routine. While the predictability of the art can be considered in determining whether an amount of experimentation is undue, mere unpredictability of the result of an experiment is not a consideration.

The instant specification, together with information that was readily available to the skilled artisan at the time the application was filed, provides a disclosure which fully enables the genus of nucleic acid molecules of claim 12.

To enable part (a) of claim 12, the specification, in conjunction with the knowledge of one skilled in the art (a M.D. or Ph.D.), must describe how to make and use a nucleotide sequence that encodes the protein of SEQ ID NO:2. Example 1 explicitly describes how the DNA encoding CKIα from *Eimeria tenella* was cloned from a sporozoite cDNA library using TgCKIα probes under low stringency conditions. The application provides the amino acid

sequence of that protein (SEQ ID NO: 2) and the encoding DNA (SEQ ID NO:1). A variety of alternate procedures for cloning a nucleotide sequence that encodes the protein of SEQ ID NO:2 are described in the specification (see, *e.g.*, p. 31, lines 8-33). One of skill in the art can easily generate additional nucleotide sequences that encode SEQ ID NO:2, taking advantage of the degeneracy of the genetic code and techniques for constructing synthetic DNA. Enablement of part (a) of claim 12 was acknowledged in the Office Action.

To enable parts (b) and (c) of claim 12, the specification, in conjunction with the knowledge of one of skill in the art, must describe how to make and use a nucleotide sequence that hybridizes under the specified stringency conditions to a second nucleic acid sequence, the complement of either SEQ ID NO: 1 or a nucleic acid molecule that encodes SEQ ID NO: 2. Importantly, of the nucleotide sequences that hybridize under the recited conditions to the second nucleic acid sequence, only those nucleotide sequences that encode a protein that is 80% identical to SEQ ID NO: 2 are encompassed by claim 12. The specification discloses SEQ ID NO: 2 (protein) and SEQ ID NO:1 (the encoding DNA). One of skill in the art, a M.D. or Ph.D., with knowledge of SEQ ID NOs:1 and 2, can easily perform hybridization experiments under the recited stringency conditions to purify nucleotide sequences that fall within parts (b) and (c) (see, *e.g.*, p.26-27 of the specification). Furthermore, one of skill in the art can easily identify which of those hybridized sequences encode a protein that is 80% identical to SEQ ID NO: 2 using standard mathematical techniques (see, *e.g.*, p. 22-23 of the specification).

Thus, a purified nucleic acid molecule of claim 12 possesses the structural characteristics described above and encodes a coccidian CKI protein, interpreted by the Office Action to mean "having any CKI 'multipotential serine/threonine protein kinase activity." The Office Action states that "[s]ince the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired multipotential serine/threonine protein kinase activity requires knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved . . . and detailed knowledge of the ways in which the protein's structure relates to its function." The Office Action states that this is not met since "the disclosure is limited to the amino acid sequence of SEQ ID NO: 2 and the nucleotide sequence of SEQ ID NO: 1." Applicants respectfully traverse this finding.

The specification discloses sequences for two additional, novel coccidian CKI proteins (TgCKIα and TgCKIβ) and, in Figure 4, compares the sequence structural features of the three novel coccidian CKI proteins to that of other CKI proteins from protozoan parasites (PfCkIα, LmCkI-2, TcCKI-2). In Figure 4, the brackets delineate the boundaries of the catalytic core region of the enzymes, representing the region of greatest homology. The specification explains

how CKI protein kinases within the family of serine/threonine protein kinases "have similar sequence domains consisting of a central kinase domain that is flanked by divergent amino- and carboxyl-terminal regions of variable lengths" (p. 15, lines 29-31), confirmed by the alignment in Figure 4. The specification further describes an internal epitope located within the catalytic domain of the three, novel coccidian CKI proteins, called "CKIα-IT" (shown in Figure 4), used to raise antisera that recognizes all three of the proteins (described in Example 2, p. 44, lines 3-30). Finally, Example 2 of the specification describes protein kinase assays to test the kinase activity of the coccidian CKI proteins. One of skill in the art can use this information to easily test whether a nucleotide sequence that falls within parts (b) and (c) of claim 12 indeed represents a coccidian CKI protein.

The leading case on enablement, In re Wands, 858 F.2d 731 (Fed. Cir. 1988), illustrates this principle. The issue in Wands was whether the specification of the Wands patent enabled production of a class of antibodies having an IgM isotype and a binding affinity of at least $10^9 M^{-1}$ using Kohler Milstein technology. Kohler Milstein technology is a classic technique that involves individualized screening of hybridomas to identify a subset with desired binding characteristics. Until the hybridomas are screened, it is unpredictable which will have the desired characteristics. Nevertheless, the court found that "[p]ractitioners of this art are prepared to screen negative hybridomas in order to find one that makes the desired antibody," and the patent was held enabled. *Id.* at 740. Regarding the claims of the instant application, and in light of the skill in the molecular biology field being very high, there is no technical difficulty in first constructing and/or identifying a nucleotide sequence that falls with the structural limitations of parts (b) and (c) of claim 12 (*i.e.*, hybridizes under the recited stringency conditions to the disclosed sequences and is 80% identical to a nucleic acid that encodes SEQ ID NO:2), and then testing the functionality of the protein encoded by said sequence.

II. Written Description

Claim 12 was additionally rejected under 35 U.S.C. § 112, 1st paragraph, for allegedly containing subject matter not sufficiently described in the application to convey that Applicants had possession of said subject matter upon application filing. The Office Action states that "[t]he specification does not contain any disclosure of the desired function of all [the] DNA sequences or the encoded polypeptides" that fall within the genus of claim 12. Applicants respectfully traverse.

Applicants argue that the specification, in combination with knowledge of those skilled in the art, show that they were in possession of the genus of nucleic acid molecules encompassed by claim 12 at the time the instant application was filed. The specification identifies sequences

encoding novel coccidian CKI proteins, including SEQ ID NOs: 1 (DNA) and 2 (the encoded protein). It further identifies the catalytic/kinase domain of SEQ ID NO:2 and compares it to similar catalytic domains of other protozoan parasite CKI proteins, including other coccidian CKI proteins newly disclosed in the instant application. One of skill in the art recognizes that conservative amino acid differences within this domain should result in a protein with the same functional attributes of SEQ ID NO: 2, even if some conservative amino acid substitutions will not preserve CKI activity. The skilled artisan will additionally recognize that the divergent amino- and carboxyl-terminal regions of SEQ ID NO:2 (as delineated in the sequence alignment in Figure 4) are more likely to tolerate mutations without affecting the functional attributes of the protein. This information provides sufficient structure/function information for one of ordinary skill in the art to conclude that Applicants possessed nucleic acid molecules that encode a protein that varies from SEQ ID NO: 2 and functions as a coccidian CKI protein.

In light of the arguments and amendments presented above, Applicants respectfully request the reconsideration of the instant enablement and written description rejections to claim 12 under 35 U.S.C. § 112, 1st paragraph.

Applicants maintain that all pending claims are in condition for allowance and a favorable action on the merits is earnestly solicited.

Respectfully submitted,

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Date: May 21, 2009